REMARKS

This Response is filed in response to the Final Office Action dated May 1, 2008. A Petition for a two month extension of time is submitted with this response. The Director is authorized to charge $460.00 for the petition for a two month extension of time, or to credit any overpayment to Deposit Account No. 02-1818. If such a withdrawal is made, please indicate the Attorney Docket No. 112701-818 on the account statement.

Claims 1-3 and 6-8 are pending in the application. In the Office Action, Claims 1-3 and 6-8 are rejected only under 35 U.S.C. § 112. For at least the reasons set forth below, Applicants respectfully submit that the rejection is improper and should be withdrawn.

In the Office Action, Claims 1-3 and 6-8 were rejected under 35 U.S.C. §112, first paragraph, for allegedly lacking enablement. Specifically, the Patent Office Action suggests that there is lack of support in the specification for compositions comprising a polynucleotide antisense to gluosylceremide synthase mRNA and compositions that treat or prevent epithelial tissue damage. In support of this contention, the Patent Office cites several reasons that there is no relation between the claimed composition and treating or preventing epithelial tissue damage. In contrast, however, it is well known and described in the specification that glucosylceramide synthase is associated with epithelial tissue damage, that the regulation of glucosylceramides in maintaining epithelial cell homeostasis is related to preventing/treating epithelial damage by silencing glucosylceramide synthase expression, and that reducing epithelial cell proliferation is related to preventing/treating epithelial damage.

Applicants disagree with the Patent Office's conclusion of lack of enablement. An analysis of whether a particular claim is supported by the disclosure in an application requires a determination of whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention. The standard for determining whether the specification meets the enablement requirement is whether the experimentation needed to practice the invention is undue or unreasonable. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). A patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). Applicants respectfully submit that, when read in view of the specification, the skilled artisan would be able to practice the claimed invention without undue experimentation.

As discussed in detail in the previously submitted response dated March 26, 2008, the survival and propagation of epidermal cells damaged and/or mutated by stress in the form of UV radiation, pollutants, free radicals, chemical substances and the like leads to epithelial tissue damage. See, Preliminary Amendment, page 4, lines 3-4 and page 8, lines 9-18. Whether the damaged cells survive and propagate depends on a balance between proliferation, differentiation and apoptosis of epidermal cells. See, Preliminary Amendment, page 7, lines 28-29. This balance is regulated by lipids. See, Preliminary Amendment, page 7, line 30. In particular, ceramides inhibit cellular proliferation and induce cellular differentiation and programmed cell death, and, conversely, glycosylceramides promote cellular proliferation and prevent cellular differentiation and programmed cell death. See, Preliminary Amendment, page 8, lines 4-6. CD_{1d} supports the continued existence of stressed cells by binding glycosylceramides. See, Preliminary Amendment, page 8, lines 7-8 and page 10, lines 13-15. Glycosylceramide synthase converts ceramides into glycosylceramides. Therefore, genetic modification or deletion of the glucosylceramide synthase mRNA to reduce the availability of glycosylceramides to CD_{1d} binding blocks the function of CD_{1d} to support the survival and propagation of damaged epidermal cells, thus preventing or treating epithelial tissue damage.

More specifically, the specification clearly states that CD_{1d} appears to negatively regulate cell apoptosis such that CD_{1d} supports a continued existence of stressed cells (*e.g.*, cells exposed to UV radiation), even when the genetic material of the cell is damaged and/or mutated, which damaged cells will continue to induction of inflammation processes and eventually account for the phenonmenom of ageing or, eventually, tumor development. See, Preliminary Amendment, page 7, line 26-page 8, line 6. Therefore, in blocking apopotosis and/or modifying endogenous CD_{1d} function, apoptosis of cells under stress may be promoted, instead of their survival and propagation. See, Preliminary Amendment, page 8, lines 14-17.

Further, the Patent Office admits that the glucosylceramide synthase mRNA sequence and antisense technology were both known in the art at the time of the invention. See, Office Action, page 3, lines 16-18. As such, it must follow that the sequence for glucosylceramide synthase was also known to be capable of binding to the glucosylceramide synthase mRNA sequence to prohibit the translation of the glucosylceramide synthase mRNA into glucosylceramide synthase.

Glucosylceramide synthase is generally known in the art to be a pivotal enzyme in the biosynthesis and catalyses the transfer of glucose from UDP-glucose (UDP-Glc) to ceramide to form glucosylceramide (GlcCer), the common precursor of most higher-order glycosphingolipids. Therefore, glucosylceramide synthase is critical to the production of GlcCer.

GlcCer is known to be a substance that is capable of blocking and/or modifying biological CD_{1d} function (*e.g.*, GlcCer is capable of blocking the CD_{1d} receptors from binding with natural killer T-cells and, thus, reduces or prevents inflammatory and/or immunosuppressive reactions). See, Preliminary Amendment, page 11, lines 5-26. The specification clearly states that "ceramides are associated with inhibition of cellular proliferation, induction of cellular differentiation and programmed cell death. In contrast, GlcCer induce cell proliferation and inhibit programmed cell death." See, Preliminary Amendment, page 7, line 26-page 8, line 6. Thus, since GlcCer is able to block and/or modify biological CD_{1d} function, GlcCer is capable of promoting apoptosis, which is desirable in instances where cells have experienced damage but are capable of proliferating to potentially cause ageing and/or tumor development. It would be beneficial, instead, for such stressed cells to be terminated to reduce or eliminate the risk of aging and/or tumor development.

Therefore, based on the above information, it must follow that an RNA polynucleotide antisense to a sequence comprising the glucosylceramide synthase mRNA is capable of binding to the glucosylceramide synthase mRNA to prohibit the formation of glucosylamide synthase, which will, in turn, reduce or eliminate the production of glucosylamide. The reduction or elimination of glucosylamide will, in turn, reduce damaged cell proliferation thereby preventing or treating epithelial tissue damage as is required, in part, by the present claims. For at least these reasons, Applicants respectfully submit that it is only with a misunderstanding of the specification and/or state of the art at the time of filing of the present application is the Examiner able to maintain the present enablement rejection.

Moreover, compliance with the enablement requirement of 35 U.S.C. §112, first paragraph, does not turn on whether an example is disclosed. An example may be "working" or "prophetic." A working example is based on work actually performed. A prophetic example describes an embodiment of the invention based on predicted results rather than work actually conducted or results actually achieved. An applicant need not have actually reduced the

invention to practice prior to filing. See, MPEP 2164.02. Therefore, Applicants respectfully submit that, even if the Patent Office is correct that there are no working examples, the present disclosure is still enabling.

While the application may not disclose working examples of tests performed using the presently claimed substances and methods with humans, Applicants respectfully submit that this is not dispositive. For example, it is generally accepted in the art that mice are proven experimental models for determinations as to possible effects of new drugs and compounds for use in humans. Further, the specification is replete with experimental data derived from experimentation with the presently claimed substances and methods and mice. The examples found at pages 54-75 support a role for CD_{1d} in the regulation of phopholipid metabolism which controls inflammatory processes. The examples also demonstrate that blocking CD_{1d} upregulates genes trolling hair follicle development, and down-regulates genes involved in inflammation and cancer development.

Therefore, based on the above information, which contains information that was known in the art and information that is disclosed in the specification, Applicants respectfully submit that the skilled artisan would be able to practice the present invention without undue experimentation.

Accordingly, Applicants respectfully submit that the rejection under 35 U.S.C. §112, first paragraph, is improper and should be withdrawn.

For the foregoing reasons, Applicants respectfully request reconsideration of the above-identified patent application and earnestly solicit an early allowance of same. In the event there remains any impediment to allowance of the claims which could be clarified in a telephonic interview, the Examiner is respectfully requested to initiate such an interview with the undersigned.

Respectfully submitted,

BELL, BOYD & LLOYD LLP

BY _____
Robert M. Barrett
Reg. No. 30,142
Customer No.: 29157
Phone No. 312-807-4204

Dated: September 29, 2008